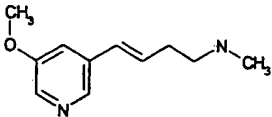
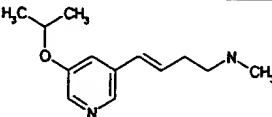
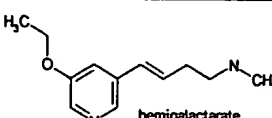
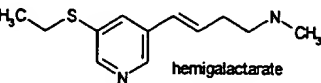




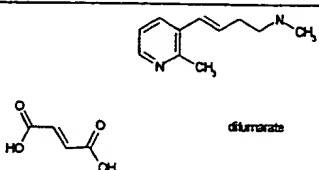
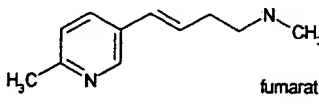
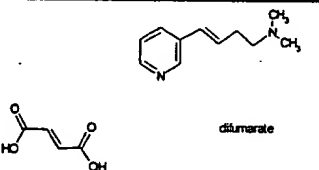
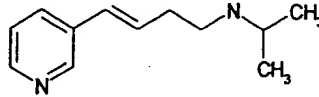
**Table 1**

Compound	STRUCTURE	Ki	Cp max (ng/mL)	AUC 0- $\infty$ (h.ng/mL)
1		9	18	23
2		5	19	30
3		5	8	12
4		28	21	24

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**Table 2**

Compound	STRUCTURE	Ki
1	 fumarate	5585
2	 fumarate	598
3	 fumarate	2067
4		270000

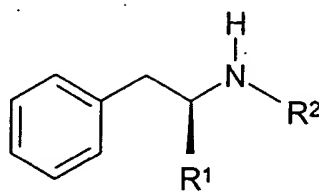
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**Table 3**

**Improved Plasma Half-life for  $\beta$ -Phenethylamine Compounds  
Having an  $\alpha$ -Methyl Group**



Species (route)	R <sup>1</sup>	R <sup>2</sup>	t <sub>1/2</sub>
Dog (i.v.)	H	H	5-10 min
Dog (i.v.)	H	CH <sub>3</sub>	5-10 min
Dog (i.v.)	CH <sub>3</sub>	H	4.5 h
Human (i.v.)	CH <sub>3</sub>	CH <sub>3</sub>	12.2 h
Human (p.o.)	CH <sub>3</sub>	CH <sub>3</sub>	10.1 h

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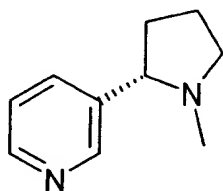
ON FILED NOV 11 2003



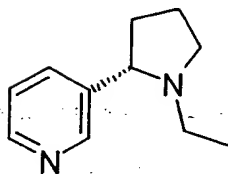
**Table 4**

**Effects of Methyl Group Substitution of (S)-(-)-Nicotine  
on the  $\alpha 4\beta 2$  Nicotinic Pharmacophore**

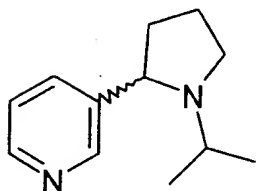
- Methyl group  $\alpha$  to N in (S)-(-)-nicotine



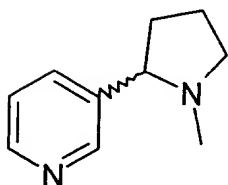
**K<sub>i</sub> = 2 nM**



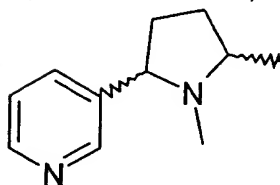
**K<sub>i</sub> = 52 nM**



**K<sub>i</sub> = 1500 nM**



**K<sub>i</sub> = 43 nM (Literature value from M.B.)**

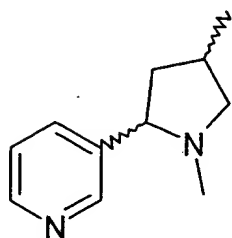


**K<sub>i</sub> = 6400 nM**

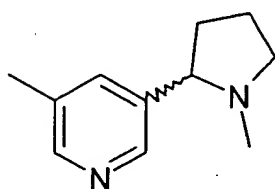
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- Methyl groups not  $\alpha$  to N in (S)-(-)-nicotine



**K<sub>i</sub> = 91 nM**



**K<sub>i</sub> = 2 nM**

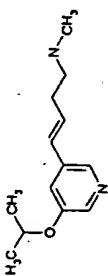
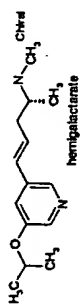
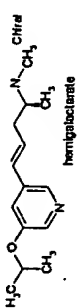
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**Table 5**

Compound	STRUCTURE	Ki	$\alpha 4\beta 2$ Emax	$\alpha 4\beta 2$ EC50	Activity Ratio Emax/EC50	Cp max (ng/mL)	AUC 0- $\infty$ (h.ng/mL)
1		5	59	379	0.15	19	30
2	 hemilactate	62	14	88	0.16	28	50
3	 hemilactate	11	57	220	0.26	39	123